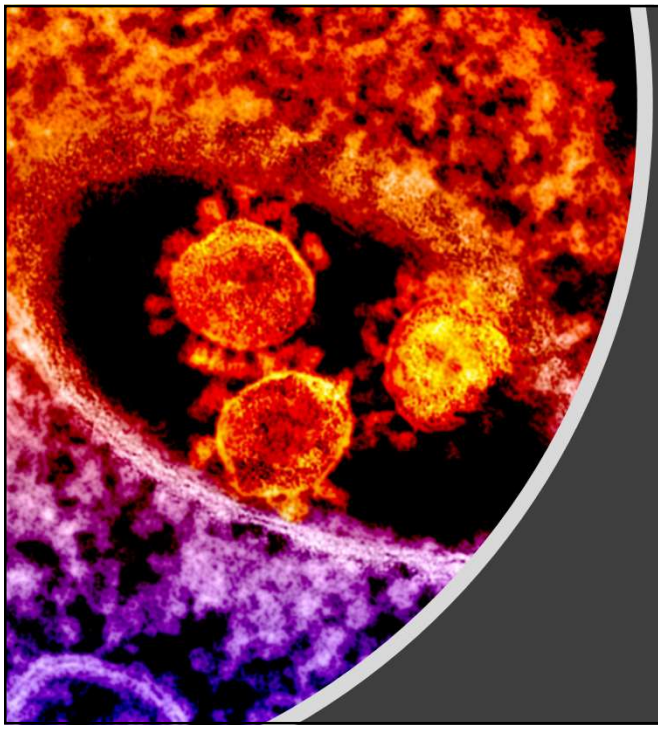


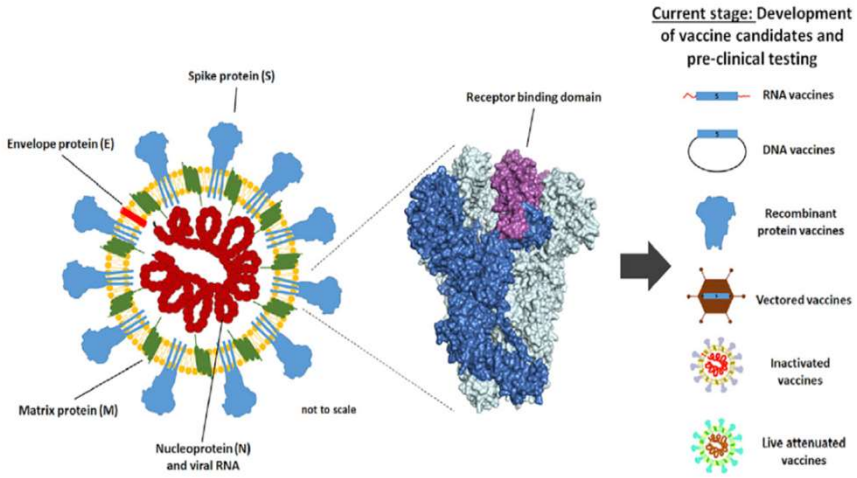
# COVID VACCINES: WHAT CAN WE EXPECT?

William Schaffner, MD
Professor of Preventive Medicine and Infectious Diseases
Vanderbilt University School of Medicine

# Disclosures

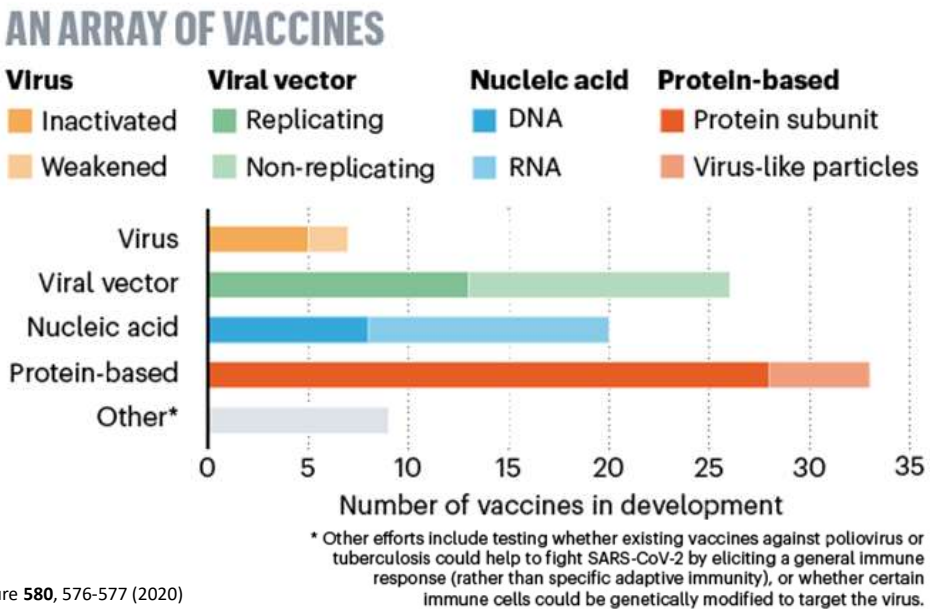
- Grant recipient
  CDC Emerging Infections Program
- Consultant
  VBI Vaccines

## Overview of Potential SARS-CoV-2 Vaccine Platforms




Immunity 52, April 14, 2020 © 2020 Elsevier Inc.

## Vaccine Approach: Strategies




Nature **580**, 576-577 (2020)

## Vaccine Update

- Over 200 COVID-19 vaccines currently under development
- Within the United States:
  - **Four** vaccines in active Phase III clinical trials
  - **Five** vaccines in active Phase I/II clinical trials

Sources: https://www.modernatx.com/cove-study; https://www.pfizer.com/science/coronavirus/vaccine, https://connect.trialscope.com/studies/34986a8a-b779-4169-a35c-5d929149d426; https://www.reuters.com/article/us-health-coronavirus-pfizer/pfizer-says-coronavirus-vaccine-study-shows-mostly-mild-to-moderate-side-effects-idUSKBN26631T

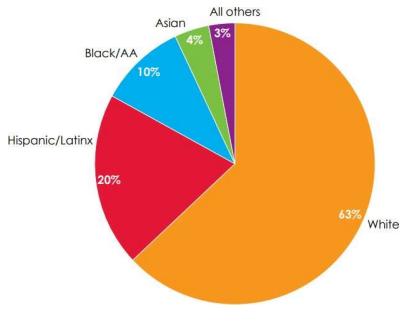
## Vaccine Update: Phase III clinical trials in the U.S.

- AZD1222 vaccine (AstraZeneca) announced removal of FDA hold 10/23, resuming Phase III trials
- Ad26.COV2.S vaccine (Janssen) announced lifting of safety pause 10/23, resuming Phase III trials
- BNT162b2 vaccine (Pfizer/BioNtech)
  - **42,133** participants enrolled as of 10/26/2020
  - 35,771 participants have received their second vaccination
  - 30% of U.S. participants enrolled have "diverse backgrounds"
- mRNA-1273 vaccine (Moderna): ***Enrollment Complete***
  - **30,000** participants enrolled as of 10/22/2020
  - 25,654 participants have received their second vaccination

Sources: https://www.modernatx.com/cove-study; https://www.pfizer.com/science/coronavirus/vaccine, https://connect.trialscope.com/studies/34986a8a-b779-4169-a35c-5d929149d426; https://www.reuters.com/article/us-health-coronavirus-pfizer/pfizer-says-coronavirus-vaccine-study-shows-mostly-mild-to-moderate-side-effects-idUSKBN26631T

# Vaccine Update: Phase III clinical trials in the U.S.

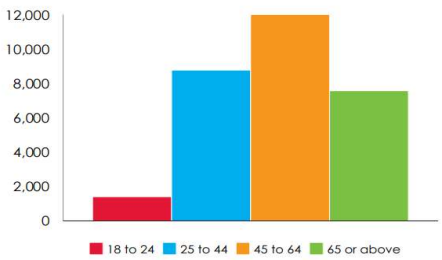
## Race and ethnicity



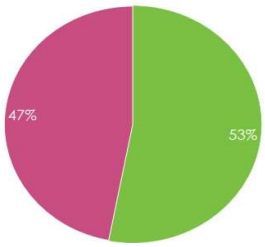

**27**% of participants living with comorbidities:
including diabetes, cardiac disease, lung disease, obesity

**22**% healthcare personnel

Cove Study age breakdown




Cove Study gender distribution




## Age and gender

moderna

Sources: https://www.modernatx.com/sites/default/files/content_documents/2020-COVE-Study-Enrollment-Completion-10.22.20.pdf

# Messenger **RNA (mRNA)**

Vital role in protein synthesis

Single-stranded molecule in nucleus

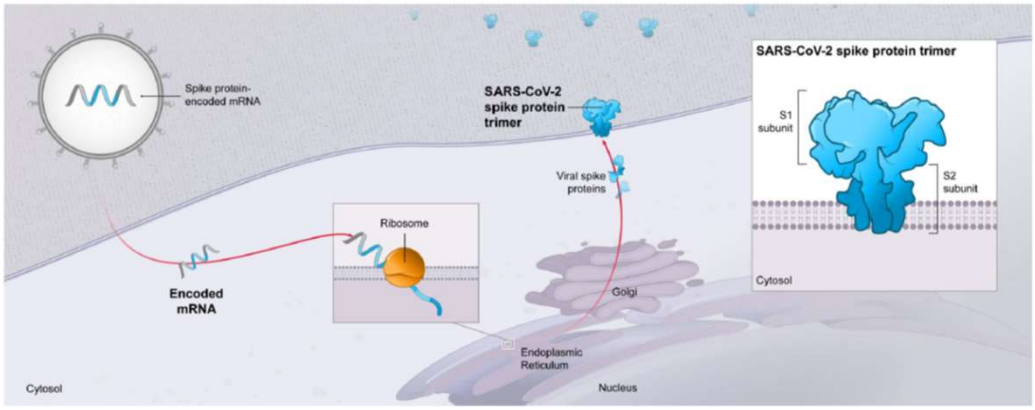
Picks up a copy of a DNA gene sequence (transcription)

Leaves nucleus, carries genetic code to ribosomes in cytoplasm

Translation of code to protein synthesis

## SARS-CoV-2 vaccine (mRNA-1273)

*Encodes for the full spike S protein*



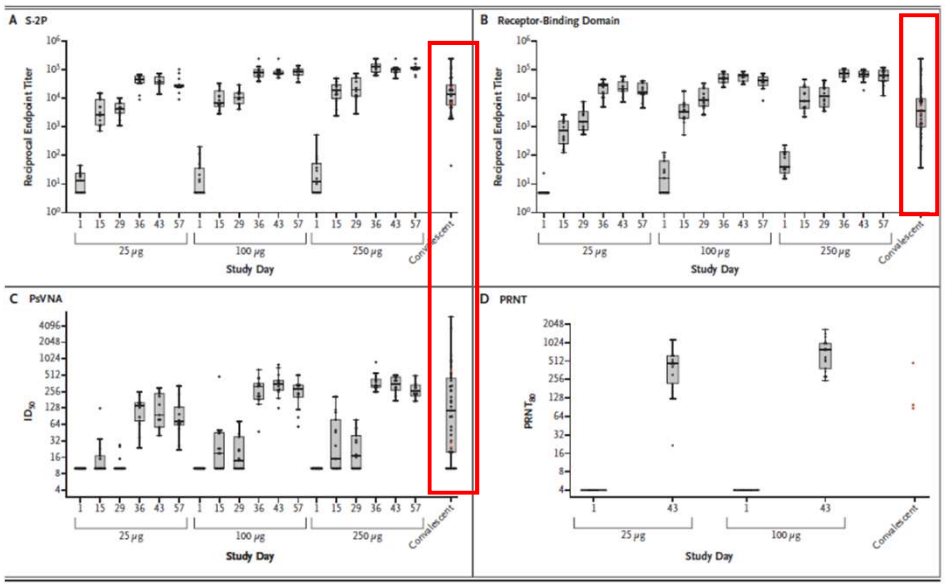

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

L.A. Jackson, E.J. Anderson, N.G. Rouphael, P.C. Roberts, M. Makhene, R.N. Coler, M.P. McCullough, J.D. Chappell, M.R. Denison, L.J. Stevens, A.J. Pruijssers, A. McDermott, B. Flach, N.A. Doria-Rose, K.S. Corbett, K.M. Morabito, S. O'Dell, S.D. Schmidt, P.A. Swanson II, M. Padilla, J.R. Mascola, K.M. Neuzil, H. Bennett, W. Sun, E. Peters, M. Makowski, J. Albert, K. Cross, W. Buchanan, R. Pikaart-Tautges, J.E. Ledgerwood, B.S. Graham, and J.H. Beigel, for the mRNA-1273 Study Group*

This article was published on July 14, 2020, at NEJM.org.

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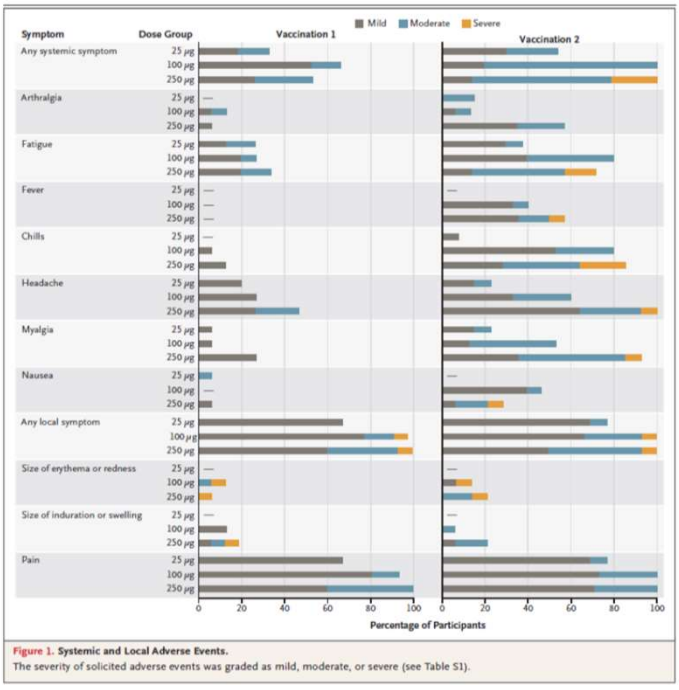


**Figure 1. Systemic and Local Adverse Events.**
The severity of solicited adverse events was graded as mild, moderate, or severe (see Table S1).

# US-Supported COVID-19 Vaccine Candidates in Clinical Evaluation: Phase 3

| Platform | Type | Doses | Developer | Timing of Phase 3 |
|---|---|---|---|---|
| RNA | LNP-mRNA | 2 | Moderna/NIAID | July |
| RNA | LNP-mRNAs | 2 | Pfizer/BioNTech | July |
| Non-replicating viral vector | ChAdOx1-S | 2 | Oxford/AZ | August |
| Non-replicating viral vector | Ad 26 | 1 | Janssen | September |
| Protein subunit | Recomb. protein/ Matrix M | 2 | Novavax | |
| Protein subunit | Recomb protein/ASO3 | 2 | Sanofi | |

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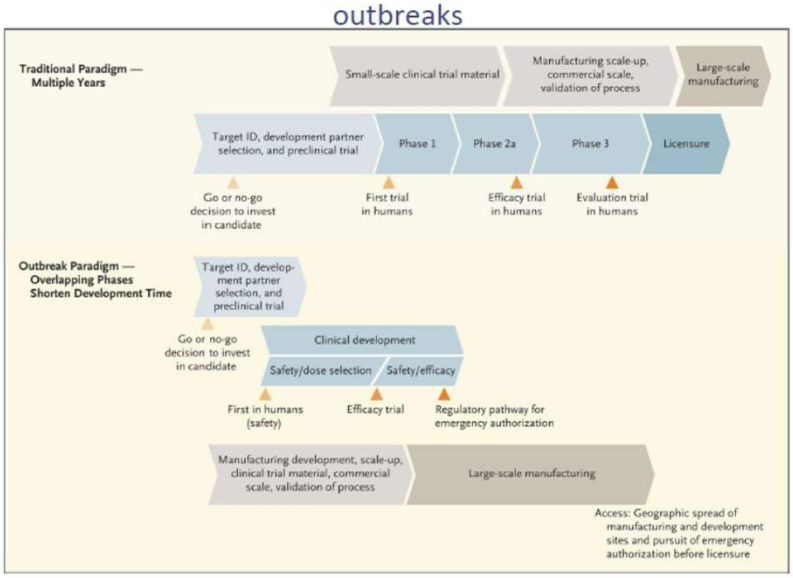
## Comparing the traditional vaccine development approach with one designed for outbreaks




Developing Covid-19 Vaccines at Pandemic Speed; new England journal of medicine
https://www.nejm.org/doi/full/10.1056/NEJMp2005630#figures_media

## COVID-19 Vaccine Clinical Development Timeline

-OWS Goal: 300M doses *with the initial doses available* by Jan 2021.

-Vaccine commercial scale manufacture proceeding "at risk"

-Clinical efficacy outcome: VE=50% (95% CI LL=30%), [interim analysis @ 32 cases (Pfizer) & 53 cases (Moderna)]

-Minimum safety f/u: median 2 months follow-up post final dose.

| | 2020 | | | | | | 2021 |
|---|---|---|---|---|---|---|---|
| VACCINE | Jul | Aug | Sep | Oct | Nov | Dec | Jan |
| Moderna | | | | | | Submit EUA? | |
| Pfizer | | | | | Submit EUA? | | |
| AstraZeneca | | | | | | | |
| Janssen | | | | | | | |
| Novavax | | | | | | ? | |

=Phase III  = Phase I or II

## FDA Guidance for Determining Vaccine Efficacy

- Minimum Efficacy 50%
- Sample Size: 30,000 of Phase 3 trials, randomized
- Primary Outcome: COVID Disease
- Secondary Outcome: More Serious Outcomes
- Close Follow-up of COVID Positives
- Subjects Enrolled: High Risk; Older adults, Chronic Conditions, Minorities
- Multiple Blood Draws To Determine Correlates of Protection
- Long-term follow up for safety

# Safety Assessments

- Meticulous Attention to Local and Systemic Reactions
  - Monitoring reactions with daily cell phone queries
  - Frequent testing for COVID 19 if symptomatic
  - Large numbers of participants recruited
  - All hospitalizations and serious reactions assessed
  - Trials halted with significant reactions
  - Independent Data and Safety Monitoring Committees Monitor Trials
- Challenges to Vaccine Assessment
  - Accelerated Development of Vaccines with New Vaccine Platforms
  - Vaccinations Occurring in a Short Time-frame with Relatively Short Follow-up Before Efficacy Signal May Be Reached

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## Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines

*Steven Black, Juhani Eskola, Claire-Anne Siegrist, Neal Halsey, Noni MacDonald, Barbara Law, Elizabeth Miller, Nick Andrews, Julia Stowe, Daniel Salmon, Kirsten Vannice, Hector S Izurieta, Aysha Akhtar, Mike Gold, Gabriel Oselka, Patrick Zuber, Dina Pfeifer, Claudia Vellozzi*

| | Number of coincident events since a vaccine dose | | | Baseline rate used for estimate |
|---|---|---|---|---|
| | Within 1 day | Within 7 days | Within 6 weeks | |
| Guillain-Barré syndrome (per 10 million vaccinated people) | 0·51 | 3·58 | 21·50 | 1·87 per 100 000 person-years (all ages; UK Health Protection Agency data) |
| Optic neuritis (per 10 million female vaccinees) | 2·05 | 14·40 | 86·30 | 7·5 per 100 000 person-years in US females (table 2)[16] |
| Spontaneous abortions (per 1 million vaccinated pregnant women) | 397 | 2780 | 16 684 | Based on data from the UK (12% of pregnancies)[34] |
| Sudden death within 1 h of onset of any symptoms (per 10 million vaccinated people) | 0·14 | 0·98 | 5·75 | Based upon UK background rate of 0·5 per 100 000 person-years (table 2)[28] |

***Table 6:*** **Predicted numbers of coincident, temporally associated events after a single dose of a hypothetical vaccine, based upon background incidence rates**

www.thelancet.com Vol 374 December 19/26, 2009

Annals of Internal Medicine ORIGINAL RESEARCH

# Attitudes Toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults

*Table 2.* Intent to Be Vaccinated, by Participant Characteristics

| Characteristic | Intent to Be Vaccinated, *n* (%) | | | *P* Value | |
|---|---|---|---|---|---|
| | Yes (*n* = 571) | Not Sure (*n* = 313) | No (*n* = 107) | Yes vs. Not Sure | Yes vs. No |
| **Age group** | | | | <0.001 | <0.001 |
| 18–29 y | 100 (49.6) | 82 (40.5) | 20 (9.9) | | |
| 30–44 y | 116 (47.0) | 91 (36.8) | 40 (16.2) | | |
| 45–59 y | 127 (52.0) | 88 (35.9) | 29 (12.1) | | |
| ≥60 y | 228 (76.5) | 53 (17.7) | 17 (5.8) | | |
| **Gender** | | | | 0.002 | 0.035 |
| Female | 263 (51.6) | 186 (36.4) | 61 (12.0) | | |
| Male | 308 (64.0) | 128 (26.5) | 46 (9.5) | | |
| **Race/ethnicity** | | | | <0.001 | <0.001 |
| Asian, non-Hispanic | 27 (77.5) | 7 (22.5) | 0 (0.0) | | |
| Black, non-Hispanic | 47 (39.3) | 48 (40.5) | 24 (20.2) | | |
| Hispanic | 72 (44.5) | 66 (40.7) | 24 (14.8) | | |
| Other, non-Hispanic | 11 (57.2) | 4 (19.6) | 5 (23.3) | | |
| Two or more races, non-Hispanic | 16 (55.5) | 10 (34.1) | 3 (10.5) | | |
| White, non-Hispanic | 398 (63.5) | 178 (28.3) | 51 (8.2) | | |
| **Educational attainment** | | | | <0.001 | <0.001 |
| No high school diploma | 45 (46.6) | 31 (32.2) | 20 (21.2) | | |
| High school graduate or equivalent | 129 (46.2) | 113 (40.6) | 37 (13.3) | | |
| Some college | 155 (56.5) | 84 (30.7) | 35 (12.8) | | |
| College graduate or above | 242 (70.9) | 85 (24.9) | 14 (4.2) | | |
| **Annual household income** | | | | 0.002 | <0.001 |
| <$30 000 | 131 (49.4) | 91 (34.3) | 43 (16.3) | | |
| $30 000 to <$60 000 | 147 (52.9) | 99 (35.5) | 32 (11.6) | | |
| $60 000 to <$100 000 | 143 (60.0) | 73 (30.7) | 22 (9.3) | | |
| ≥$100 000 | 150 (71.1) | 50 (24.1) | 9 (4.3) | | |

Ann Intern Med. doi:10.7326/M20-3569

Annals of Internal Medicine ORIGINAL RESEARCH

# Attitudes Toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults

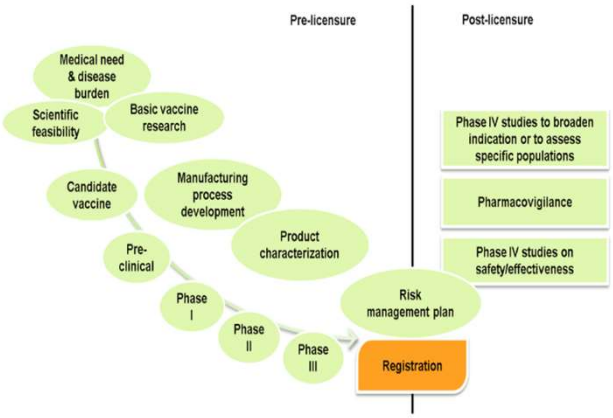
*Table 4.* Reasons Participants Provided for Responding "No" or "Not Sure" Regarding Intent to Be Vaccinated*

| Theme and Subtheme | Intent to Be Vaccinated | |
|---|---|---|
| | Not Sure (*n* = 220) | No (*n* = 83) |
| **Specific concerns about the vaccine** | **126 (57.3)** | **21 (25.3)** |
| Side effects, safety | 75 (34.1) | 14 (16.9) |
| Efficacy | 43 (19.5) | 2 (2.4) |
| Newness, including not wanting to be the first to get the vaccine | 37 (16.8) | 7 (8.4) |
| Rigor of testing | 11 (5.0) | 1 (1.2) |
| Vaccine contents | 3 (1.4) | 3 (3.6) |
| **Need additional information** | **49 (22.3)** | **2 (2.4)** |
| Compatibility with personal health conditions (e.g., allergies, comorbid conditions) | 15 (6.8) | 1 (1.2) |
| Recommendation from doctor or official | 6 (2.7) | 0 (0.0) |
| Timing regarding state of pandemic, personal immunity | 7 (3.2) | 1 (1.2) |
| Need more information, unspecified | 30 (13.6) | 0 (0.0) |
| **Antivaccine attitudes, beliefs, and emotions** | **44 (20.0)** | **47 (56.6)** |
| Don't need the vaccine (e.g., not at risk) | 7 (3.2) | 5 (6.0) |
| Religious beliefs | 0 (0.0) | 3 (3.6) |
| Don't believe the vaccine will work, informed by reference to other bad vaccine experiences, flu shot not working, vaccine won't work against mutating organism | 10 (4.5) | 7 (8.4) |
| General statements about not getting vaccines | 6 (2.7) | 7 (8.4) |
| Don't believe in, want, or feel comfortable with vaccines | 5 (2.3) | 18 (21.7) |
| Fear about vaccines | 3 (1.4) | 5 (6.0) |
| Misconceptions, or incorrect information about vaccines | 19 (8.6) | 11 (13.3) |
| **Lack of trust** | **28 (12.7)** | **27 (32.5)** |
| Vaccines | 4 (1.8) | 4 (4.8) |
| Government and the CDC | 4 (1.8) | 5 (6.0) |
| Pharmaceutical companies | 0 (0.0) | 1 (1.2) |
| Vaccine development or testing processes | 11 (5.0) | 2 (2.4) |
| Reference to specific conspiracy theories | 6 (2.7) | 6 (7.2) |
| Distrust unspecified | 2 (1.0) | 13 (15.7) |
| **Other** | **19 (8.6)** | **1 (1.2)** |
| Altruism, wanting higher risk individuals to get vaccine first | 4 (1.8) | 0 (0.0) |
| Cost | 12 (5.5) | 0 (0.0) |
| Dislike of needles | 5 (2.3) | 1 (1.2) |

Ann Intern Med. doi:10.7326/M20-3569

# Vaccine Confidence and Communication

- **Strong Science is a Necessary Starting Point**
- **Health Care Worker Confidence in and Commitment to Vaccines is a Necessary Starting Point**
- **Trust in the Process is Paramount**




http://www.mdpi.com/2076-393X/1/3/204/htm

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# FDA Vaccine and Related Biological Products Advisory Committee (VRBPAC)

Median 2 month follow-up
- Too brief for efficacy eval

- Too brief for safety
  - 2 mos EUA; 6 mos BLA

Mild disease in relatively healthy population
- Serious disease
- Duration of protection

Continued blinding after EUA?

## Post – EUA Safety Evaluation

FDA: BEST-links CMS data with other "big data"

CDC: VAERS – safety signals

Clinical Immunization Safety Assessment (CISA)

Rapid cycle analysis

V-SAFE – smartphone electronic health check

## COVID Vaccine Implementation Issues

Vaccine distribution

Vaccine storage/handling

- Pfizer -80°C
- Moderna -20°C

Lead federal agency: OWS or CDC

Prioritization of vaccines

Vaccine registries

Vaccine costs

- Vaccine free (OWS)
- Administration fee – traditional payors

Communication

- To medical/public health professionals
- To general public

## Striving for Herd Immunity

Proportion of population vaccinated X vaccine effectiveness

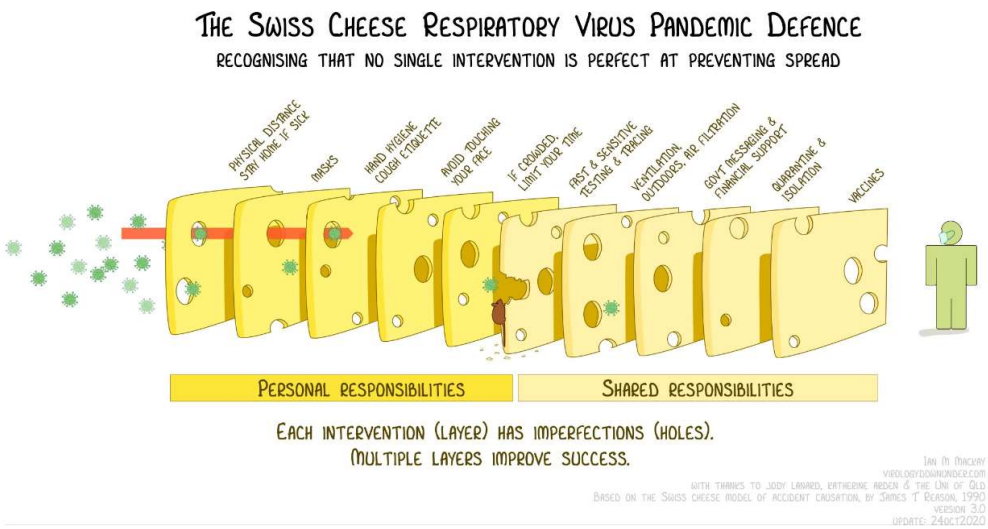
66% x 70% = 46% protected

## The Continuing Need for Behavioral Interventions Even After COVID Vaccination

There will be many susceptibles for a long time:

- Vaccine NOT 100% effective

  Therefore, some vaccinees remain susceptible!
- Vaccines require 2 doses (quite reactogenic)
- Will take months to vaccinate 300+ million
- Many will decline/put off vaccination
- Duration of protection unknown




# Thank You!

Your questions, suggestions and corrections are appreciated.